

CLAIMS

1. A transgenic mouse comprising:

a first transgenic nucleotide sequence, integrated into the genome of said mouse, encoding human amyloid precursor protein (hAPP) operably linked to a first promoter; and

a second transgenic nucleotide sequence, integrated into the genome of said mouse, encoding human (h) α -synuclein operably linked to a second promoter;

wherein the first and second transgenic nucleotide sequences are expressed, and wherein, as a result of said expression, said transgenic mouse develops neurodegenerative disease.

2. The transgenic mouse of claim 1, wherein said first promoter comprises a platelet-derived growth factor β (PDGF- β) promoter.

3. The transgenic mouse of claim 2, wherein a simian virus (SV)40 derived intron operably links said PDGF- β promoter to said first transgenic nucleotide sequence.

4. The transgenic mouse of claim 1, wherein said first promoter comprises a Thy1 promoter.

5. The transgenic mouse of claim 1, wherein said first promoter comprises a

prion (PrP) promoter.

20 6. The transgenic mouse of claim 1, wherein said first promoter comprises a PDGF- β promoter.

22 7. The transgenic mouse of claim 6, wherein a SV40 derived intron operably links said PDGF- β promoter to said second transgenic nucleotide sequence.

24 8. The transgenic mouse of claim 1, wherein said second promoter comprises a Thy1 promoter.

26 9. The transgenic mouse of claim 1, wherein said second promoter comprises a PrP promoter.

28 10. The transgenic mouse of claim 1, wherein said second promoter comprises a PDGF- β promoter.

30 11. The transgenic mouse of claim 10, wherein a SV40 derived intron operably links said PDGF- β promoter to said second transgenic nucleotide sequence.

32 12. The transgenic mouse of claim 1, wherein proteins encoded by the first and second transgenic nucleotide sequences are overexpressed as compared to a

34 non-transgenic mouse of the same strain.

13. The transgenic mouse of claim 1, wherein the nucleotide sequence of
36 hAPP comprises introns between exons 6 through 9 of hAPP.

14. The transgenic mouse of claim 1, wherein the nucleotide sequence
38 encoding hAPP encodes hAPP770.

15. The transgenic mouse of claim 1, wherein the nucleotide sequence
40 encoding hAPP encodes hAPP751.

16. The transgenic mouse of claim 1, wherein the nucleotide sequence
42 encoding hAPP encodes hAPP695.

17. The transgenic mouse of claim 1, wherein the hAPP is a mutant hAPP.

44 18. The transgenic mouse of claim 17, wherein the nucleotide sequence
encoding the mutant hAPP encodes a protein that contains a change from lysine to
46 asparagine at amino acid 670 and a change from methionine to leucine at amino acid
671.

48 19. The transgenic mouse of claim 17, wherein the nucleotide sequence

encoding the mutant hAPP encodes a protein that contains a change from valine to
isoleucine at amino acid 717.

20. The transgenic mouse of claim 17, wherein the nucleotide sequence
encoding the mutant hAPP encodes a protein that contains a change from valine to
phenylalanine at amino acid 717.

21. The transgenic mouse of claim 1, wherein the nucleotide sequence
encoding hAPP encodes only a portion of hAPP.

22. The transgenic mouse of claim 21, wherein hAPP is A β ₁₋₄₂.

23. The transgenic mouse of claim 1, wherein the nucleotide sequence of α -
synuclein comprises a coding sequence of α -synuclein.

24. The transgenic mouse of claim 1, wherein the h α -synuclein is a mutant
h α -synuclein.

25. The transgenic mouse of claim 24, wherein the nucleotide sequence
encoding the mutant h α -synuclein encodes a protein that contains a change from
alanine to proline at amino acid 30.

64 26. The transgenic mouse of claim 24, wherein the nucleotide sequence
encoding the mutant h α -synuclein encodes a protein that contains a change from
66 alanine to threonine at amino acid 53.

 27. A transgenic mouse comprising:
68 a first transgenic nucleotide sequence, integrated into the genome of said
mouse, encoding human amyloid precursor protein (hAPP) operably linked to a platelet
70 derived growth factor β (PDGF- β) promotor operably linked to a simian virus (SV)40
intron;
72 a second transgenic nucleotide sequence, integrated into the genome of said
mouse, encoding human (h) α -synuclein operably linked to a PDGF- β promoter
74 operably linked to an SV40 intron;
 wherein the first and second transgenic nucleotide sequences are expressed,
76 and wherein, as a result of said expression, said transgenic mouse develops
neurodegenerative disease.

78 28. The transgenic mouse of claim 27, wherein proteins encoded by the first
and second transgenic nucleotide sequences are overexpressed as compared to a
80 non-transgenic mouse of the same strain.

 29. The transgenic mouse of claim 27, wherein the hAPP comprises a coding
82 sequence containing introns between exons 6 through 9.

30. The transgenic mouse of claim 27, wherein the hAPP contains a mutation
of valine to isoleucine at amino acid 717.

31. The transgenic mouse of claim 27, wherein h α -synuclein comprises the
coding sequence of h α -synuclein.

32. The transgenic mouse of claim 27, wherein neurodegenerative disease
comprises formation of intraneuronal inclusions characteristic of Lewy body disease.

33. The transgenic mouse of claim 27, wherein neurodegenerative disease
comprises formation of fibrillary Lewy body-like inclusions.

34. The transgenic mouse of claim 27, wherein neurodegenerative disease
comprises neuronal death.

35. The transgenic mouse of claim 27, wherein neurodegenerative disease
comprises development of motor deficits.

36. The transgenic mouse of claim 27, wherein age of onset of
neurodegenerative disease occurs at a significantly ($p < 0.05$) younger age than in
singly transgenic littermates.

37. A method for screening therapeutic agents for the prevention or treatment
of neurological disease comprising administration of therapeutic interventions to a
transgenic mouse comprising:

a first transgenic nucleotide sequence, integrated into the genome of said
mouse, encoding human amyloid precursor protein (hAPP) operably linked to a first
promoter;

a second transgenic nucleotide sequence, integrated into the genome of said
mouse, encoding human (h) α -synuclein operably linked to a second promoter;

wherein the first and second transgenic nucleotide sequences are expressed,
and wherein, as a result of said expression, said transgenic mouse develops
neurodegenerative disease.